

Benzodiazepines in Clinical Practice

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1. Description
 - ❖ Belong to a group of central nervous system (CNS) depressants
 - ❖ Classified in Controlled Substances Act (CSA) as Schedule IV
 - ❖ Used therapeutically to produce sedation, induce sleep, relieve anxiety and muscle spasms and to prevent seizures
 - ❖ Act as hypnotics in high doses
 - ❖ Act as anxiolytics in moderate doses
 - ❖ Act as sedatives in low doses
 - ❖ 15 members of this group are presently marketed in the United States
 - ❖ About 20 additional benzodiazepines are marketed in other countries
 - ❖ Should not be used to relieve nervousness or tension caused by stress of everyday life
 - ❖ Used to treat insomnia – not effective for more than a few weeks
 - ❖ May be habit-forming especially when taken for a long time or in high doses
 - ❖ Presence of other medical problems may affect use of benzodiazepines:
 - ❖ Alcohol abuse [or history of]
 - ❖ Drug abuse or dependence [or history of] – dependence on benzodiazepines may be more likely to develop
 - ❖ Epilepsy or history of seizures – although some benzodiazepines are used in treating epilepsy, starting or suddenly stopping treatment may increase seizures
2. Benzodiazepine Prescriptions
 - ❖ Most widely prescribed by non-physicians
 - ❖ 1.3 billion prescriptions between 1965 – 1985
 - ❖ 1965 mostly Librium
 - ❖ 1975 mostly Valium
 - ❖ 1987 mostly Xanax
 - ❖ 100 million prescriptions in 1999
3. Ambivalence and Benzodiazepines
 - ❖ Benzodiazepine use in US is widespread
 - ❖ Society remains ambivalent regarding its use
 - ❖ Fear of physician over-prescribing
 - ❖ Normal anxiety vs. pathologic anxiety
 - ❖ Psychotherapist's view of anxiety as useful
 - ❖ Influence of pharmaceutical industry
 - ❖ Culture of medicating normal feelings
4. Psychiatric Indications for Benzodiazepine Prescribing
 - ❖ Anxiety
 - ❖ Panic disorder
 - ❖ Insomnia
5. Less Accepted Psychiatric Indications for Prescribing
 - ❖ Treatment of depression
 - ❖ Augment neuroleptics in schizophrenia
 - ❖ Treat neuroleptic side-effects

6. Medical Indications for Benzodiazepine Prescribing
 - ❖ Acute seizures
 - ❖ Anesthetic
 - ❖ Muscle relaxant
 - ❖ Anxiety & agitation with medical illness
 - ❖ Treatment of alcohol and benzodiazepine withdrawal
7. Topology of Benzodiazepine use
 - ❖ Therapeutic use as directed by prescription
 - ❖ Unsupervised therapeutic misuse
 - ❖ Drug abusers taking benzodiazepines to treat effects of other drugs (e.g., cocaine, heroin)
 - ❖ Drug dependents on benzodiazepines only to get high
 - ❖ Polydrug dependent persons (e.g., methadone & benzodiazepine dependence) to get high
8. Therapeutic Use as Directed
 - ❖ Prescribed only after careful assessment
 - ❖ Specific diagnosis in mind
 - ❖ Alternatives to benzodiazepine pharmacotherapy explored
 - ❖ Treatment duration discussed
 - ❖ Patient does not exceed dosage
 - ❖ Discontinuation considered
9. Unsupervised Therapeutic Misuse
 - ❖ Patient increases dose on their own
 - ❖ Ex-patient had some benzodiazepines left over & uses them intermittently without physician approval
 - ❖ People obtain benzodiazepines from friends/relatives
 - ❖ Taken in response to perceived need
10. Drug Abusers' Uses of Benzodiazepines
 - ❖ Used by heroin dependent persons if they are sick and can't get opioids
 - ❖ Used by cocaine dependent persons if they are feeling too edgy after cocaine binge
 - ❖ Used by persons who are dependent on benzodiazepines alone
 - ❖ Used by persons on methadone maintenance to get high due to drug interaction
11. To prescribe or not to prescribe?
 - ❖ Clear indication
 - ❖ Lack of alternative therapies
 - ❖ Negative patient & family history of alcoholism or drug dependence
 - ❖ Patient medication monitor available
 - ❖ Look for signs of abuse: lost prescriptions, self-adjustment of medication such as 'using ahead,' intoxication
12. Risk-Benefit Discussion
 - ❖ Acute drug toxicity
 - ❖ Chronic drug toxicity
 - ❖ Dependency with Discontinuation symptoms

13. Benzodiazepine's Side Effects
 - ❖ Drowsiness
 - ❖ Ataxia
 - ❖ Dysarthria
 - ❖ Diplopia
 - ❖ Vertigo & falls
 - ❖ Hostility & depression
 - ❖ Memory effects
14. At Risk Groups for Dependence
 - ❖ Prior history of Sedative Hypnotic or Alcohol Dependence
 - ❖ Chronic medically ill (consider SSRI and/or psychosocial treatments)
 - ❖ Chronic psychiatrically ill
 - ❖ Dysthymia or Borderline Personality
 - ❖ Chronic insomnia
15. Pharmacologic Options to Benzodiazepines
 - ❖ SSRI antidepressants
 - ❖ Tri-cyclic antidepressants
 - ❖ Low dose neuroleptics
 - ❖ Buspirone
 - ❖ Zolpidem
16. Non-Pharmacologic Options
 - ❖ Psychotherapy
 - ❖ Biofeedback
 - ❖ Mediation
 - ❖ Acupuncture
 - ❖ Social support
 - ❖ Sleep hygiene
 - ❖ Caffeine & nicotine discontinuation
17. Benzodiazepine Intoxication
 - ❖ Unsteady gait
 - ❖ Slurred speech
 - ❖ Impaired judgment
 - ❖ Vertical & horizontal nystagmus
 - ❖ Similar to alcohol intoxication (with negative alcohol breath and urine test and positive benzodiazepine urine test)

Benzodiazepine Discontinuation Syndromes

18. Benzodiazepine Withdrawal
 - ❖ Can occur after abrupt discontinuation even at therapeutic doses
 - ❖ Serious withdrawal can occur after more than one month of benzodiazepine use at twice therapeutic dose
 - ❖ Signs & symptoms may not follow a specific course
 - ❖ Onset & duration depend on half-life of benzodiazepine
19. Very Frequent Benzodiazepine Withdrawal Symptoms
 - ❖ Anxiety
 - ❖ Insomnia
 - ❖ Restlessness
 - ❖ Agitation
 - ❖ Irritability
 - ❖ Muscle tension
20. Common but Less Frequent Symptoms
 - ❖ Nausea
 - ❖ Diaphoresis
 - ❖ Coryza [acute rhinitis]
 - ❖ Lethargy
21. Uncommon Symptoms
 - ❖ Psychosis
 - ❖ Seizures
 - ❖ Tinnitus
 - ❖ Delirium
 - ❖ Hallucinations
22. Factors that predispose to Seizures
 - ❖ High dose
 - ❖ Longer duration
 - ❖ Shorter half-life of benzodiazepine
 - ❖ Abrupt discontinuation
 - ❖ Polydrug or alcohol abuse
 - ❖ Medications that lower seizure threshold
 - ❖ Latent seizures
23. Characteristics of Seizures
 - ❖ Mostly grand mal type
 - ❖ Shorter half-life of benzodiazepine cause quicker onset (e.g., 1-3 days after Xanax® but 1-2 weeks with Valium®)
24. How to reduce Discontinuation Symptoms
 - ❖ Gradual dose tapering of same agent
 - ❖ Substitute long-acting benzodiazepine for short acting benzodiazepine (e.g., Valium® or clonazepam for alprazolam)
 - ❖ Substitute a non-benzodiazepine (e.g., phenobarbital, tegretol)

25. Relapse Prevention
- ❖ Recognize high risk situations
 - ❖ Coping skills for negative emotions
 - ❖ Coping skills for social pressures
 - ❖ Lifestyle changes for a balanced life
 - ❖ 12 step involvement
 - ❖ Cue recognition
 - ❖ Plan to interrupt a slip

Sedatives and Hypnotics

Benzodiazepines

- ❖ Dalmane
- ❖ Doral
- ❖ *Estazolam* [ProSom]
- ❖ *Flurazepam* [Dalmane]
- ❖ Halcion
- ❖ ProSom
- ❖ Quazepam [Doral]
- ❖ Restoril
- ❖ *Temazepam* [Restoril]
- ❖ *Triazolam* [Halcion]

Barbiturates

- ❖ Mebaral
- ❖ *Mephobarbital* [Mebaral]
- ❖ Nembutal
- ❖ *Pentobarbital* [Nembutal]
- ❖ Phenobarbital
- ❖ *Secobarbital* [Seconal]
- ❖ Seconal

Miscellaneous Sedatives and Hypnotics

- ❖ Ambien
- ❖ Atarax
- ❖ Hydroxyzine [Atarax]
- ❖ Phenergan
- ❖ Promethazine [Phenergan]
- ❖ Sonata
- ❖ *Zaleplon* [Sonata]
- ❖ *Zolpidem* [Ambien]

Anti-anxiety Agents [Benzodiazepines and combinations]

- ❖ *Alprazolam* [Xanax]
- ❖ *Amitriptyline with Chlordiazepoxide* [Limbitrol]
- ❖ Ativan
- ❖ *Chlordiazepoxide* [Librium]
- ❖ *Clorazepate* [Tranxene]
- ❖ *Diazepam* [Valium]
- ❖ Librium

Anti-anxiety Agents [Benzodiazepines and combinations] continued

- ❖ Limbitrol
- ❖ *Lorazepam* [Ativan]
- ❖ *Oxazepam* [Serax]
- ❖ Serax
- ❖ Tranxene
- ❖ Valium
- ❖ Xanax

Miscellaneous Anti-anxiety Agents

- ❖ *Amitriptyline with perphenazine* [Triavil]
- ❖ Atarax
- ❖ BuSpar
- ❖ *Buspirone* [BuSpar]
- ❖ *Doxepin* [Sinequan]
- ❖ Effexor XR [Effexor]
- ❖ *Escitalopram* [Lexapro]
- ❖ *Hydroxyzine* [Atarax]
- ❖ Lexapro
- ❖ *Meprobamate* [Miltown]
- ❖ *Paroxetine* [Paxil]
- ❖ Paxil
- ❖ Prochlorperazine
- ❖ *Sertraline* [Zoloft]
- ❖ Sinequan
- ❖ Stelazine [Trifluoperazine]
- ❖ Triavil
- ❖ Trifluoperazine
- ❖ *Venlafaxine* [Effexor]
- ❖ *Vistaril* [Atarax]
- ❖ Zoloft

Longer duration benzodiazepines used to treat insomnia:

alprazolam (Xanax®)
chlordiazepoxide (librium®)
clorazepate (Tranxene®)
diazepam (Valium®)
halazepam (Paxipam®)
lorazepam (Ativan®)
oxazepam (Serax)
prazepam (Centrax®)
quazepam (Doral®)

Benzodiazepines used as anticonvulsants:

Clonazepam (Klonopin®)
Diazepam (Valium®)
Clorazepate (Tranxene®)

Flunitrazepam (Rohypnol®) is a benzodiazepine that is not manufactured or legally marketed in the US but is smuggled in by traffickers

In mid-1990s, was extensively trafficked in Florida and Texas

Known as “roopies,” “roofies,” and “roach” popular as “party” drug by younger individuals
Also been utilized as a “date rape” drug – in this context, it is placed in an alcoholic drink which incapacitates and prevents resistance from sexual assault; victim unaware of what happened and does not report

Zolpidem (Ambien®) and zaleplon (Sonata®) are relatively new benzodiazepine-like CNS depressants that have been approved for short-term treatment of insomnia; both share same properties as benzodiazepines and are in Schedule IV of CSA